

## REMARKS

Applicants have cancelled claim 8 and non-elected claims 12-20, and reserve the right to pursue the subject matter of the canceled claims in one or more continuing applications.

Applicants have also added eleven new claims, i.e., claims 21-31. Support for claims 21-22, 24-25, and 27-29 can be found in seven original claims, i.e., claims 4-7 and 9-11, respectively, support for claims 23 and 31 can be found in original claim 5, and support for claims 26 and 30 can be found in the Specification, page 8, line 4. Applicants have further amended claims 1, 4-7, and 9 to promote clarity, amended claim 4 to delete the terms "animal" and "plant," amended claim 10 to revise its dependency (as necessitated by the cancellation of claim 8), and amended claim 11 to replace "DMEM-LG" with "Dulbecco's modified Eagle's medium containing 1 g/L of glucose." Support for the replacement in claim 11 can be found in the Specification, page 8, lines 22-25. Finally, Applicants have also amended the Specification to describe FIGs. 3, 5, and 6 in a more lucid manner. No new matter has been introduced.

Claims 1-7, 9-11, and 21-29 are currently pending. Reconsideration of the application, as amended, is respectfully requested in view of the remarks below.

### Declaration

The Examiner asserts that the previously filed Declaration is defective. See the Office Action, page 2. Applicants will address this issue after this application has been allowed.

### Objections

Objections have been made to the Specification and claim 11. See the Office Action, pages 3-4. Pursuant to the Examiner's requests, Applicants have amended the Specification to more clearly describe FIGs. 3, 5, and 6, and amended claim 11 to replace the recited abbreviation "DMEM-LG."

### Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 4-11 under 35 U.S.C. § 112, second paragraph, as being indefinite. See the Office Action, page 3. Applicants submit that this rejection has been overcome by the above amendments.

Rejection under 35 U.S.C. § 102

Claims 1-5 and 7-10 are rejected under 35 U.S.C. § 102(b) as being obvious over Lucas *et al.* (Wound Repair and Regeneration (1995) 3: 449-460). See the Office Action, page 4. Applicants disagree.

Claim 1, the only independent claim, will be first discussed.

Claim 1 is drawn to a method for recovering mesenchymal stem cells. The method includes steps: (i) providing a mixture containing mesenchymal stem cells; (ii) **seeding** the mixture into a culture device; and (iii) culturing the mesenchymal stem cells. Note that the culture device is used for **seeding** mesenchymal stem cells. For example, when the culture device contains a plate with pores, the seeding step includes adhering the mesenchymal stem cells to the plate while passing smaller size cells (e.g., haematopoietic stem cells) through the pores. See the Specification, page 8, line 28 to page 9, line 10.

According to the Examiner, Lucas *et al.* teaches “a method of recovering mesenchymal stem cells (MSC) comprising obtaining a mixture comprising mesenchymal stem cells from rat leg muscle tissue, seeding the mixture into a culture device. ... The MSC were recovered by **filtering** the culture from the culture device through a 20 micro filter to separate the MSC from myotubes” (emphasis added). See the Office Action, page 4, lines 9-14.

Applicants would like to point out that the **filtering** step disclosed in Lucas *et al.* involves **passing** desired mesenchymal stem cells through a device (i.e., a 20 µm Nitex filter) to remove larger size cells such as myotubes. See Lucas *et al.*, page 450, right column, lines 21-25. Clearly, Lucas *et al.* teaches **passing** mesenchymal stem cells through a filter. In contrast, claim 1 requires the steps of **seeding** the mesenchymal stem cells into a culture device and subsequently culturing them in the culture device. Thus, contrary to the Examiner's assertion, Lucas *et al.* does not teach **seeding** a mixture containing mesenchymal stem cells into a culture device, as required by claim 1. It, therefore, does not anticipate claim 1. Claims 2-5 and 7-10, each dependent from claim 1 directly or indirectly, are not anticipated by Lucas *et al.* either.

For the reasons set forth above, Applicants request this rejection be withdrawn.

Rejection under 35 U.S.C. § 103

Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lucas *et al.* in view of Bruder *et al.* (US Patent No. 5,942,225). See the Office Action, pages 4-5.

The Examiner allegedly asserts that "it would have been obvious to one of ordinary skill in the art to use mammalian MSC [as taught by Bruder *et al.*] in the method taught by Lucas *et al.* ..." See the Office Action, page 5, lines 12-14. Applicants disagree.

As discussed above, claim 1, the only independent claim, is drawn to a method for recovering mesenchymal stem cells. Lucas *et al.* does not teach or suggest seeding a mixture containing mesenchymal stem cells into a culture device. Rather, Lucas *et al.* teaches passing mesenchymal stem cells through a filtering device. In other words, Lucas *et al.* teaches away from seeding mesenchymal stem cells into a culture device and subsequently culturing them in the culture device, which are required by claim 1. The secondary reference, Bruder *et al.*, only teaches a method for directing human mesenchymal stem cells cultivated in vitro to differentiate into specific cell lineages prior to their implantation for therapeutic treatment. As a result, Lucas *et al.* and Bruder *et al.* in combination teach away claim 1, as well as claims 2-11 dependent from it. Thus, claims 1-11 are not rendered obvious by the two cited references.

CONCLUSION

For the reasons set forth above, Applicants submit that the grounds for the rejections asserted by the Examiner have been overcome, and that the claims, as pending, define subject matter that is novel and nonobvious over the prior art.

Applicants submit that all of the claims are now in condition for allowance, which action is requested. Pursuant to 37 CFR § 1.136, applicant hereby petitions that the period for response to the action dated November 23, 2002, be extended for one month to and including March 23, 2002. Enclosed is a check for \$ 55 for the required fee.

Attached is a marked-up version of the changes being made by the current amendment.

Applicant : Shih-Chieh Hung et al.  
Serial No. : 09/761,893  
Filed : January 17, 2001  
Page : 8


Attorney's Docket No.: 12862-002001 / 0674-5737US

Please apply any other charges to Deposit Account No. 06-1050, referencing 12862-002001.

Respectfully submitted,

Date: \_\_\_\_\_

3-22-02

  
Y. Rocky Tsao, Ph.D., J.D.  
Attorney for Applicants  
Reg. No. 34,053

Fish & Richardson P.C.  
225 Franklin Street  
Boston, Massachusetts 02110-2804  
Telephone: (617) 542-5070  
Facsimile: (617) 542-8906

20387582.doc

**VERSION WITH MARKINGS TO SHOW CHANGES MADE**

In the specification:

Paragraph beginning at page 6, line 1 has been amended as follows:

[FIG. 3] FIG. 3(a) and FIG. 3(b) [is a diagram showing] show osteogenic induction of human mesenchymal cell cultures[, wherein the cells show]. Cells in the induction group exhibited [varying degrees] a higher degree of positive stain for alkaline phosphatase [in induction group] as shown in FIG. 3(a) [as compared to] than cells in the control[s] as shown in FIG. 3(b).

Paragraphs beginning at page 6, lines 8 have been amended as follows:

[FIG. 5] FIG. 5(a) and FIG. 5(b) [is a diagram showing] show adipogenic differentiation of mesenchymal cell cultures[, wherein the cells show]. Cells in the induction group exhibited [varying degrees] a higher degree of positive stain for Oil-red O [in induction group] as shown in FIG. 5(a) [as compared to] than cells in the control[s] as shown in FIG. 5(b) after induction for 7 days.

[FIG. 6] FIG. 6(a) and FIG. 6(b) [is a diagram showing] show chondrogenic differentiation of mesenchymal cell cultures[, wherein cells show]. Cells exhibited chondrocyte morphology in Safranin-O stain as shown in FIG. 6(a) [(a)]; and toluidine blue stain as shown in FIG. 6(b) [(b)] after induction for 21 days.

In the claims:

Claims 1 and 4-7 have been amended as follows:

1. (Amended) A method for recovering mesenchymal stem cells, comprising:
  - (a) providing a mixture comprising mesenchymal stem cells;
  - (b) seeding the mixture into a culture device; and
  - (c) [recovering and] culturing the mesenchymal stem cells.

4. (Amended) The method as claimed in claim 1, wherein the mixture comprises [cells selected from the group consisting of mammals and animals, and plants] mammalian mesenchymal stem cells.

5. (Amended) The method as claimed in claim 4, wherein the cells are selected from the group consisting of fractionated tissue[s], un-fractionated tissue[s], [bloods,] and a body fluid[s].

6. (Amended) The method as claimed in claim 5, wherein the [mammal] mixture comprises human mesenchymal stem cells.

7. (Amended) The method as claimed in claim 5, wherein the cells are selected from the group consisting of a bone marrow, an embryonic yolk sac, a placenta, an umbilical cord, and a fetal, adolescent [and] or adult body fluid[s], and a fetal, adolescent or adult tissue[s].

Claim 8 has been cancelled.

Claims 9-11 have been amended as follows:

9. (Amended) The method as claimed in claim 1 [8], wherein the mesenchymal stem cells are [can] differentiable [differentiate] into tissues comprising bone, adipose, or cartilage.

10. (Amended) The method as claimed in claim 1 [8], wherein the mesenchymal stem cells are characterized by CD 34.

11. (Amended) The method as claimed in claim 9, wherein the mesenchymal stem cells are cultured in [DMEM-LG medium containing] 10% fetal bovine serum-supplemented Dulbecco's modified Eagle's medium containing 1 g/L of glucose.

Claims 12-20 have been cancelled.